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L14: Entry 2 of 7

File: USPT

Oct 23, 2001

DOCUMENT-IDENTIFIER: US 6306820 B1

TITLE: Combination therapy using a TNF binding protein for treating TNF-mediated diseases

Detailed Description Paragraph Right (164):

An animal model of rheumatoid arthritis induced by an adjuvant was used to investigate the combination therapy of a TNF binding protein and methotrexate in male Lewis rats (3-7/group) weighing at least 200 g.

Detailed Description Paragraph Right (169):

An animal model of rheumatoid arthritis induced by an adjuvant was used to investigate the combination therapy of a TNF binding protein and methotrexate in male Lewis rats (5-7/group) weighing at least 200 g.

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L14: Entry 3 of 7

File: USPT

Aug 7, 2001

DOCUMENT-IDENTIFIER: US 6270766 B1

TITLE: Anti-TNF antibodies and methotrexate in the treatment of arthritis and crohn's disease

Detailed Description Paragraph Right (10):

The benefits of combination therapy with methotrexate and TNF antagonists include high clinical response rates for significantly longer durations in comparison with that obtained with treatment with each therapeutic modality separately. In addition, methotrexate significantly reduces immunogenicity of anti-TNF antibodies, thus permitting administration of multiple dosages of anti-TNF antibodies with enhanced safety. The results described herein suggest that methotrexate can be used to reduce immunogenicity of other antibodies or proteins. Based on the results described herein, methotrexate can be used in other forms of antibody therapy, such as anti-IL-2 antibody therapy. This method is particularly pertinent in therapies other than anti-CD4 antibody therapy.